CLAIMS:

1. A method of analyzing a biological sample of an organism for chromosomal deletions or amplifications associated with cancer, the biological sample including nucleic acid molecules originating from normal cells and potentially from cells associated with cancer, wherein at least some of the nucleic acid molecules are cell-free in the biological sample, the method comprising:

determining first and second haplotypes for normal cells of the organism at a first chromosomal region, the first chromosomal region including a first plurality of loci, wherein the first and second haplotypes are heterozygous at each of the first plurality of loci;

for each of a plurality of the nucleic acid molecules in the biological sample:

identifying a location of the nucleic acid molecule in a reference genome of the organism; and

determining a respective allele of the nucleic acid molecule;

identifying a first group of nucleic acid molecules as being from the first haplotype based on the identified locations and determined alleles, the first group including at least one nucleic acid molecule located at each of the first plurality of loci;

identifying a second group of nucleic acid molecules as being from the second haplotype based on the identified locations and determined alleles, the second group including at least one nucleic acid molecule located at each of the first plurality of loci;

calculating, with a computer system, a first value of the first group of nucleic acid molecules, the first value defining a property of the nucleic acid molecules of the first group;

calculating, with the computer system, a second value of the second group of nucleic acid molecules, the second value defining a property of the nucleic acid molecules of the second group; and

comparing the first value to the second value to determine a classification of whether the first chromosomal region exhibits a deletion or an amplification in any cells associated with cancer.

2. The method of claim 1, wherein the first chromosomal region is classified as exhibiting a deletion or an amplification in cells associated with cancer, and wherein the cells associated with cancer include a malignant tumor and/or from a premalignant lesion.

3. The method of claim 1, wherein each locus of the first plurality of loci is at least 500 bases apart from another locus of the first plurality of loci.

4. The method of claim 1, wherein the comparison includes determining a difference between the first value and the second value, and wherein the classification includes comparing the difference to at least one threshold value.

5. The method of claim 4, wherein the at least one threshold value is derived from a healthy organism or from a region not having a deletion or amplification, wherein the sequential probability ratio testing, the t-test, or the chi-square test is used to determine the at least one threshold value.

6. The method of claim 1, wherein the first value corresponds to a statistical value of a size distribution of the nucleic acid molecules of the first group, and the second value corresponds to a statistical value of a size distribution of the nucleic acid molecules of the second group.

7. The method of claim 6, wherein the first value is an average size of the nucleic acid molecules of the first group, and the second value is an average size of the nucleic acid molecules of the second group.

8. The method of claim 6, wherein the first value Q_{HapI} is a fraction of nucleic acid molecules in the first group that are shorter than a cutoff size, and the second value Q_{HapII} is a fraction of nucleic acid molecules in the second group that are shorter than the cutoff size.

9. The method of claim 8, wherein the comparison includes determining a difference between the first value and the second value, wherein the difference is $\Delta Q = Q_{HapI} - Q_{HapII}$, and wherein a positive value of ΔQ greater than a threshold value indicates that the second haplotype includes a deletion in tumor tissue in the organism or that the first haplotype includes an amplification in tumor tissue in the organism.

10. The method of claim 8, wherein the comparison includes determining a difference between the first value and the second value, wherein the difference is $\Delta Q = Q_{HapI} -$

Q_{HapII}, and wherein an approximate value of zero for ΔQ indicates that no deletion or amplification exists in the first chromosomal region.

11. The method of claim 6, wherein the first value $F_{Hap\ I}$ and the second value $F_{Hap\ II}$ are defined for a respective haplotype as $F = \sum^{w}length / \sum^{N}length$, where $\sum^{w}length$ represents a sum of lengths of the nucleic acid molecules of the corresponding group with a length equal to or less than a cutoff size w; and $\sum^{N}length$ represents a sum of lengths of the nucleic acid molecules of the corresponding group with a length equal to or less than N bases, where N is greater than w.

12. The method of claim 11, wherein the difference is $\Delta F = F_{Hap\ I} - F_{Hap\ II}$, and wherein a positive value of ΔF greater than a threshold value indicates that the second haplotype includes a deletion in tumor tissue in the organism.

13. The method of claim 11, wherein the difference is $\Delta F = F_{Hap\ I} - F_{Hap\ II}$, and wherein a negative value of ΔF greater than a threshold value indicates that the second haplotype includes an amplification in tumor tissue in the organism.

14. The method of claim 1, wherein the first value of the first group corresponds to a number of nucleic acid molecules located at the first plurality of loci, and the second value of the second group corresponds to a number of nucleic acid molecules located at the first plurality of loci.

15. The method of claim 14, further comprising:

calculating a ratio of the first value and the second value to determine a fractional concentration of cancer DNA in the biological sample.

16. The method of claim 15, further comprising:

determining the fractional concentration of cancer DNA in the biological sample at a plurality of times; and

using the fractional concentration at the plurality of times to diagnose, stage, prognosticate, or monitor progress of a level of cancer in the organism.

17. The method of claim 1, further comprising:

for each of a plurality of other chromosomal regions:

repeating the method of claim 1;

determining a first number of chromosomal regions that exhibit a deletion or an amplification; and

comparing the first number to one or more threshold values to determine a level of cancer in the organism.

18. The method of claim 17, further comprising:

determining an amount of deletion or amplification for each chromosomal region that was identified as exhibiting a deletion or an amplification; and

comparing the amount to one or more threshold values to determine the level of cancer in the organism.

19. The method of claim 17, further comprising:

repeating the method of claim 17 at a plurality of times; and

using the first number at the plurality of times to diagnose, stage, prognosticate, or monitor progress of the level of cancer in the organism.

20. The method of claim 19, wherein using the first number at the plurality of times to diagnose, stage, prognosticate, or monitor progress of the level of cancer in the organism includes determining the presence or progress of a premalignant condition.

21. The method of claim 17, wherein each of the chromosomal regions are of predetermined length.

22. A method of analyzing a biological sample of an organism, the biological sample including nucleic acid molecules originating from normal cells and potentially from cells associated with cancer, wherein at least some of the nucleic acid molecules are cell-free in the biological sample, the method comprising:

identifying a plurality of non-overlapping chromosomal regions of the organism, each chromosomal region including a plurality of loci;

for each of a plurality of nucleic acid molecules in a biological sample of the organism:

identifying a location of the nucleic acid molecule in a reference genome of the organism;

for each chromosomal region,

identifying a respective group of nucleic acid molecules as being from the chromosomal region based on the identified locations, the respective group including at least one nucleic acid molecule located at each of the plurality of loci of the chromosomal region;

calculating, with a computer system, a respective value of the respective group of nucleic acid molecules, the respective value defining a property of the nucleic acid molecules of the respective group; and

comparing the respective value to a reference value to determine a classification of whether the chromosomal region exhibits a deletion or an amplification; and

determining an amount of chromosomal regions classified as exhibiting a deletion or amplification.

23. The method of claim 22, further comprising:

comparing the amount to a threshold value to determine a classification of whether the organism has cancer.

24. The method of claim 22, wherein each of the chromosomal regions are of predetermined length.

25. The method of claim 22, wherein the plurality of non-overlapping chromosomal regions span the genome of the organism.

26. A method of determining a progress of chromosomal aberrations in an organism using biological samples including nucleic acid molecules originating from normal cells and potentially from cells associated with cancer, wherein at least some of the nucleic acid molecules are cell-free in the biological samples, the method comprising

identifying one or more non-overlapping chromosomal regions of a reference genome of the organism, each chromosomal region including a plurality of loci;

at each of a plurality of times:

for each of a plurality of nucleic acid molecules in a biological sample of the organism:

identifying a location of the nucleic acid molecule in the reference genome;

for each chromosomal region,

identifying a respective group of nucleic acid molecules as being from the chromosomal region based on the identified locations, the respective group including at least one nucleic acid molecule located at each of the plurality of loci of the chromosomal region;

calculating, with a computer system, a respective value of the respective group of nucleic acid molecules, the respective value defining a property of the nucleic acid molecules of the respective group;

comparing the respective value to a reference value to determine a classification of whether the first chromosomal region exhibits a deletion or an amplification; and

using the classifications of each of the chromosomal regions at the plurality of times to determine the progress of the chromosomal aberrations in the organism.

27. The method of claim 26, wherein the classification is a numerical value that reflects a difference between the respective value and the reference value for each chromosomal region at each time.

28. The method of claim 26, wherein one or more non-overlapping chromosomal regions are a plurality of chromosomal regions.

29. The method of claim 28, further comprising:

at each of the plurality of times:

determining an amount of chromosomal regions classified as exhibiting a deletion or amplification; and

wherein the amounts are used to monitor the progress of a cancer in the organism.

30. The method of claim 26, wherein the reference value is obtained from a group of nucleic acid molecules identified as being from a reference chromosomal region that does not exhibit a deletion or amplification at the time the nucleic acid molecules were obtained.

31. The method of claim 26, further comprising:

determining first and second haplotypes for normal cells of the organism at a first chromosomal region of the one or more non-overlapping chromosomal regions, the first

chromosomal region including a first plurality of loci, wherein the two haplotypes are heterozygous at each of the first plurality of loci,

wherein the respective value of the first chromosomal region is obtained from a first group of nucleic acid molecules identified as being from the first haplotype, and

wherein the reference value of the first chromosomal region is obtained from a second group of nucleic acid molecules identified as being from the second haplotype.

32. A computer program product comprising a computer readable medium storing a plurality of instructions for controlling a processor to perform an operation for methods described herein, the instructions comprising the steps of any of the claims above.

33. A computer system including processors that are programmed to implement any of the methods of any of claims above.

CLAIMS:

1. A method of analyzing a biological sample of an organism for chromosomal deletions or amplifications associated with cancer, the biological sample including nucleic acid molecules originating from normal cells and potentially from cells associated with cancer, wherein at least some of the nucleic acid molecules are cell-free in the biological sample, the method comprising:

determining first and second haplotypes for normal cells of the organism at a first chromosomal region, the first chromosomal region including a first plurality of loci, wherein the first and second haplotypes are heterozygous at each of the first plurality of loci;

for each of a plurality of the nucleic acid molecules in the biological sample:

identifying a location of the nucleic acid molecule in a reference genome of the organism; and

determining a respective allele of the nucleic acid molecule;

identifying a first group of nucleic acid molecules as being from the first haplotype based on the identified locations and determined alleles, the first group including at least one nucleic acid molecule located at each of the first plurality of loci;

identifying a second group of nucleic acid molecules as being from the second haplotype based on the identified locations and determined alleles, the second group including at least one nucleic acid molecule located at each of the first plurality of loci;

calculating, with a computer system, a first value of the first group of nucleic acid molecules, the first value defining a property of the nucleic acid molecules of the first group;

calculating, with the computer system, a second value of the second group of nucleic acid molecules, the second value defining a property of the nucleic acid molecules of the second group; and

comparing the first value to the second value to determine a classification of whether the first chromosomal region exhibits a deletion or an amplification in any cells associated with cancer.

2. The method of claim 1, wherein the first chromosomal region is classified as exhibiting a deletion or an amplification in cells associated with cancer, and wherein the cells associated with cancer include a malignant tumor and/or from a premalignant lesion.

3. The method of claim 1 or claim 2, wherein each locus of the first plurality of loci is at least 500 bases apart from another locus of the first plurality of loci.

4. The method of any one of claims 1 to 3, wherein the comparison includes determining a difference or a ratio between the first value and the second value, and wherein the classification includes comparing the difference or the ratio to at least one threshold value.

5. The method of claim 4, wherein the at least one threshold value is derived from a healthy organism or from a region not having a deletion or amplification, wherein the sequential probability ratio testing, the t-test, or the chi-square test is used to determine the at least one threshold value.

6. The method of any one of claims 1 to 5, wherein the first value corresponds to a statistical value of a size distribution of the nucleic acid molecules of the first group, and the second value corresponds to a statistical value of a size distribution of the nucleic acid molecules of the second group.

7. The method of claim 6, wherein the first value is an average size of the nucleic acid molecules of the first group, and the second value is an average size of the nucleic acid molecules of the second group.

8. The method of claim 6, wherein the first value Q_{HapI} is a fraction of nucleic acid molecules in the first group that are shorter than a cutoff size, and the second value Q_{HapII} is a fraction of nucleic acid molecules in the second group that are shorter than the cutoff size.

9. The method of claim 8, wherein the comparison includes determining a difference between the first value and the second value, wherein the difference is $\Delta Q = Q_{HapI} - Q_{HapII}$, and wherein a positive value of ΔQ greater than a threshold value indicates that the second haplotype includes a deletion in tumor tissue in the organism or that the first haplotype includes an amplification in tumor tissue in the organism.

10. The method of claim 8, wherein the comparison includes determining a difference between the first value and the second value, wherein the difference is $\Delta Q = Q_{HapI} -$

Q_{HapII}, and wherein an approximate value of zero for ΔQ indicates that no deletion or amplification exists in the first chromosomal region.

11. The method of claim 6, wherein the first value $F_{Hap\ I}$ and the second value $F_{Hap\ II}$ are defined for a respective haplotype as $F = \sum^{w}length / \sum^{N}length$, where $\sum^{w}length$ represents a sum of lengths of the nucleic acid molecules of the corresponding group with a length equal to or less than a cutoff size w; and $\sum^{N}length$ represents a sum of lengths of the nucleic acid molecules of the corresponding group with a length equal to or less than N bases, where N is greater than w.

12. The method of claim 11, wherein the comparison includes determining a difference between the first value and the second value, and wherein the difference is $\Delta F = F_{Hap\ I} - F_{Hap\ II}$, and wherein a positive value of ΔF greater than a threshold value indicates that the second haplotype includes a deletion in tumor tissue in the organism.

13. The method of claim 11, wherein the comparison includes determining a difference between the first value and the second value, and wherein the difference is $\Delta F = F_{Hap\ I} - F_{Hap\ II}$, and wherein a negative value of ΔF greater than a threshold value indicates that the second haplotype includes an amplification in tumor tissue in the organism.

14. The method of any one of claims 1 to 5, wherein the first value of the first group corresponds to a number of nucleic acid molecules located at the first plurality of loci, and the second value of the second group corresponds to a number of nucleic acid molecules located at the first plurality of loci.

15. The method of claim 14, further comprising:

calculating a ratio of the first value and the second value to determine a fractional concentration of cancer DNA in the biological sample.

16. The method of claim 15, further comprising:

determining the fractional concentration of cancer DNA in the biological sample at a plurality of times; and

using the fractional concentration at the plurality of times to diagnose, stage, prognosticate, or monitor progress of a level of cancer in the organism.

17. The method of any one of claims 1 to 16, further comprising:

for each of a plurality of other chromosomal regions:

repeating the method of claim 1;

determining a first number of chromosomal regions that exhibit a deletion or an amplification; and

comparing the first number to one or more threshold values to determine a level of cancer in the organism.

18. The method of claim 17, further comprising:

determining an amount of deletion or amplification for each chromosomal region that was identified as exhibiting a deletion or an amplification; and

comparing the amount to one or more threshold values to determine the level of cancer in the organism.

19. The method of claim 17, further comprising:

repeating the method of claim 17 at a plurality of times; and

using the first number at the plurality of times to diagnose, stage, prognosticate, or monitor progress of the level of cancer in the organism.

20. The method of claim 19, wherein using the first number at the plurality of times to diagnose, stage, prognosticate, or monitor progress of the level of cancer in the organism includes determining the presence or progress of a premalignant condition.

21. The method of claim 17, wherein each of the chromosomal regions are of predetermined length.

22. A method of analyzing a biological sample of an organism, the biological sample including nucleic acid molecules originating from normal cells and potentially from cells associated with cancer, wherein at least some of the nucleic acid molecules are cell-free in the biological sample, the method comprising:

identifying a plurality of non-overlapping chromosomal regions of the organism, each chromosomal region including a plurality of loci;

for each of a plurality of nucleic acid molecules in a biological sample of the organism:

identifying a location of the nucleic acid molecule in a reference genome of the organism;

for each of the plurality of non-overlapping chromosomal regions:

identifying a respective group of nucleic acid molecules as being from the chromosomal region based on the identified locations, the respective group including at least one nucleic acid molecule located at each of the plurality of loci of the chromosomal region;

calculating, with a computer system, a respective value of the respective group of nucleic acid molecules, the respective value defining a property of the nucleic acid molecules of the respective group; and

comparing the respective value to a reference value to determine a classification of whether the chromosomal region exhibits a deletion or an amplification;

determining an amount of chromosomal regions classified as exhibiting a deletion or amplification; and

comparing the amount to a threshold value to determine a classification of whether the organism has cancer.

23. The method of claim 22, wherein each of the chromosomal regions are of predetermined length.

24. The method of claim 22 or claim 23, wherein the plurality of non-overlapping chromosomal regions span the genome of the organism.

25. The method of any one of claims 22 to 24, wherein a chromosomal region is classified as exhibiting a deletion or an amplification only when the chromosomal region is included in at least a specified number of consecutive chromosomal regions hat have the respective value exceed the reference value, the specified number being two or more.

26. The method of any one of claims 22 to 25, wherein the threshold value has a value of at least one, and wherein comparing the amount to the threshold value indicates determining whether the amount is greater than the threshold value.

27. A method of determining a progress of chromosomal aberrations in an organism using biological samples including nucleic acid molecules originating from normal

cells and potentially from cells associated with cancer, wherein at least some of the nucleic acid molecules are cell-free in the biological samples, the method comprising

identifying one or more non-overlapping chromosomal regions of a reference genome of the organism, each chromosomal region including a plurality of loci;

at each of a plurality of times:

for each of a plurality of nucleic acid molecules in a biological sample of the organism:

identifying a location of the nucleic acid molecule in the reference genome;

for each of the one or more non-overlapping chromosomal regions,

identifying a respective group of nucleic acid molecules as being from the chromosomal region based on the identified location, the respective group including at least one nucleic acid molecule located at each of the plurality of loci of the chromosomal region;

calculating, with a computer system, a respective value of the respective group of nucleic acid molecules, the respective value of defining a property of the nucleic acid molecules of the respective group;

comparing the respective value to a reference value to determine a classification of whether the first chromosomal region exhibits a deletion or an amplification; and

using the one or more classifications of the one or more chromosomal regions at the plurality of times to determine the progress of the chromosomal aberrations in the organism by:

calculating a numerical change in classifications from one time to another time; and

comparing the numerical change to a threshold value.

28. The method of claim 27, wherein the classification is a numerical value that reflects a difference between the respective value and the reference value for each chromosomal region at each time.

29. The method of claim 27 or claim 28, wherein one or more non-overlapping chromosomal regions are a plurality of chromosomal regions.

30. The method of claim 29, further comprising:

at each of the plurality of times:

determining an amount of chromosomal regions classified as exhibiting a deletion or amplification; and

wherein the amounts are used to monitor the progress of a cancer in the organism.

31. The method of any one of claims 27 to 30, wherein the reference value is obtained from a group of nucleic acid molecules identified as being from a reference chromosomal region that does not exhibit a deletion or amplification at the time the nucleic acid molecules were obtained.

32. The method of any one of claims 27 to 30, further comprising:

determining first and second haplotypes for normal cells of the organism at a first chromosomal region of the one or more non-overlapping chromosomal regions, the first chromosomal region including a first plurality of loci, wherein the two haplotypes are heterozygous at each of the first plurality of loci,

wherein the respective value of the first chromosomal region is obtained from a first group of nucleic acid molecules identified as being from the first haplotype, and

wherein the reference value of the first chromosomal region is obtained from a second group of nucleic acid molecules identified as being from the second haplotype

33. A computer program product comprising a computer readable medium storing a plurality of instructions for controlling a processor to perform an operation for methods described herein, the instructions comprising the steps of any of the claims above.

34. A computer system including processors that are programmed to implement any of the methods of claims above.